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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/076,934	02/15/2002	Richard M. O'Hara JR.	GNN-028	3689

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LAHIVE & COCKFIELD, LLP.  
28 STATE STREET  
BOSTON, MA 02109

EXAMINER
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OUSPENSKI, ILIA I

ART UNIT	PAPER NUMBER
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1644

DATE MAILED: 12/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

10/076,934

Applicant(s)

O'HARA ET AL.

Examiner

ILIA OUSPENSKI

Art Unit

1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 02 November 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) 5,13 and 21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4, 6-12, 14-20, 22-24 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 02/19/2002 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 10/28/02, 8/4/03.
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: \_\_\_\_\_.

## DETAILED ACTION

1. Claims 1 – 24 are pending.

2. Applicant's election without traverse of Invention of Group I, Claims 1 – 4, 6 – 12, 14 – 20, and 22 – 24, drawn to a method of therapeutically or prophylactically downmodulating an autoimmune response in a subject by administering an antigen binding portion of an anti-CD28 antibody, in the reply filed on 11/02/2004, is acknowledged.

Applicant further elects the species of type I diabetes for prosecution of the merits.

2. Claims 5, 13, and 21 (non-elected Group II) are withdrawn from further consideration by the Examiner, under 37 C.F.R. § 1.142(b), as being drawn to non-elected inventions.

*Claims 1 – 4, 6 – 12, 14 – 20, and 22 – 24, as they read on type I diabetes, are under consideration in the instant application.*

3. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. The provisional application USSN 60/269,756 upon which priority is claimed appears to provide adequate support under 35 U.S.C. 112 for subject matter claimed in the instant application, except for the claimed limitation of "fully human" antibodies.

Consequently, claims 4, 12, and 20 have been accorded the priority of the filing date of the instant application, i.e. 02/15/2002.

Should Applicant disagree with the Examiner's factual determination above, it is incumbent upon Applicant to provide a showing that specifically supports the instant claim limitations.

4. Applicant's IDS, filed 10/28/2002 and 08/04/2003, are acknowledged, and have been considered.

However, references A2, A5, A6, B2, and B6 of 10/28/2002 could not be located in the instant file, and have been crossed out. Applicant is invited to resubmit these references to complete the instant file. The examiner apologizes for any inconvenience to applicant for having to resubmit these documents.

5. The use of trademarks has been noted in this application (e.g. Cremophor EL™ on page 43). Each letter of the trademarks should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

6. The specification is objected to for the following informalities: The specification includes a statement on page 48, first paragraph, that "in contrast to whole anti-CD28 antibody, PV1-scFv surprisingly prevents disease onset," however, Examples 1 – 4 on pages 48 – 49 apparently do not reference a "whole anti-CD28 antibody." Example 1 mentions "anti-CD28 (PV1.10.17)," but the nature of the referenced compound is unclear. Figures 3 – 4 mention "710-Fab," yet it is unclear what this designation refers to. Furthermore, Example 4 and Figure 4 mention "control mice," but the nature of treatment, if any, received by control mice is not disclosed.

Appropriate correction or clarification is required.

Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

7. The Drawings are objected to for the following informalities:

A. Figures 1 – 4 are not identified with Figure Numbers.

B. In Figure 1, the designations found on the graph, such as "PV1 12130RU" or "mCD28.Fc," are not sufficiently explained in the text, and it is unclear what they refer to.

Appropriate correction or clarification is required.

Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

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8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

*(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.*

*(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.*

9. Claims 1, 2, 6 – 10, and 14 – 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Linsley et al. (US Pat. 5,521,288, see entire document) as evidenced by Paul (Fundamental Immunology, 1999, page 451).

Linsley et al. teach that monoclonal antibodies to CD28 can be employed to treat various autoimmune disorders, including diabetes mellitus (see entire document, In particular, column 36 lines 36 – 43).

Since the instant claim language recites a method "comprising administering an antigen binding portion of an anti-CD28 antibody," it follows that in administering an intact antibody molecule, as taught by Linsley et al., the antigen binding portion would inherently also be administered.

Claims 6, 7, 14, and 15 are included, because, as evidenced by Paul (page 451 right column), CD28 is expressed on both CD4<sup>+</sup> and CD8<sup>+</sup> T cells. Therefore, an antibody that blocks signaling via CD28 would inherently downmodulate immune response mediated by both CD4<sup>+</sup> and CD8<sup>+</sup> T cells.

Thus the reference teaching anticipates the claimed invention.

10. Claim 1 – 4, 6 – 12, 14 – 20, and 22 – 24 are/is rejected under 35 U.S.C. 102(e) as being anticipated by Yu et al. (US Pat. Pub. 2002/0006403, see entire document) as evidenced by Paul (Fundamental Immunology, 1999, page 451).

Yu et al. teach inhibiting an immune response in a subject by administering an anti-CD28 antibody (see entire document, in particular, claim 1 and paragraph 0013). The subject may have an autoimmune disease, such as diabetes mellitus (claims 15 and 16, and paragraph 0013). The antibody may be human or humanized (claims 8 and 10, and paragraph 0012), and may consist of an antigen binding region, such as Fab or scFv (paragraph 0118).

Claims 6, 7, 14, and 15 are included, because, as evidenced by Paul (page 451 right column), CD28 is expressed on both CD4<sup>+</sup> and CD8<sup>+</sup> T cells. Therefore, an antibody that blocks signaling via CD28 would inherently downmodulate immune response mediated by both CD4<sup>+</sup> and CD8<sup>+</sup> T cells.

The reference teaching thus anticipates the claimed invention.

**11. Conclusion: no claim is allowed.**

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILIA OUSPENSKI whose telephone number is 571-272-2920. The examiner can normally be reached on Monday-Friday 9 - 5.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ILIA OUSPENSKI

Patent Examiner

Art Unit 1644

December 17, 2004

*Phillip Gambel*

PHILLIP GAMBEL, PH.D

PRIMARY EXAMINER

*TECH CENTER 1600*

*12/20/04*